AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph at page 1 directly preceding the "Background of the Invention" section, which was added pursuant to Applicant's Amendment and Response dated April 1, 2003, with the following amended paragraph:

Related Applications

This application claims priority to U.S. Provisional Application No.: 60/192,727, filed on March 27, 2001~~, incorporated by reference herein in its entirety~~.

Please replace the paragraph at page 8, lines 4-13, with the following amended paragraph:

Accordingly, the present invention is based on the discovery that FcαRI-expressing Kupffer cells, which represent a crucial cell population at the interface of mucosal and systemic immunity, are capable of mediating efficient phagocytosis of serum IgA-antigen (e.g., ~~baceria~~ bacteria) complexes. Furthermore, although both serum IgA and SIgA (though to a much lesser extent) initiated respiratory burst activity, only serum IgA was able to initiate phagocytosis. This is in agreement with a more passive role of SIgA, but attributes a significant function for serum IgA in immunity. Therefore, whereas SIgA's main function is the prevention of bacterial entrance, FcαRI-serum IgA interactions on Kupffer cells provide a second line of defense in mucosal immunity.

Please replace the paragraph at page 18, lines 12-32, with the following amended paragraph:

Serum IgA, but not secretory IgA initiates FcαRI- mediated phagocytosis. Despite increasing interest in this area, interactions of secretory versus serum IgA with effector cells remain poorly understood. Several conflicting reports describe either the ability or disability of SIgA to trigger functions like phagocytosis (Kerr, M.A. *Biochem. J. 271,* 285-296 (1990); Weisbart, R.H, *et al. Nature 332,* 647-648 (1988); Nikolova, E.B. *et al. J. Leukoc. Biol. 57,* 875-882 (1995); Gorter, A. *et al. Immunology 61,* 303-309 (1987)). Well-defined and commercially available serum and SIgA preparations showed similar binding ability *to E coli* bacteria, while no contamination with IgG Ab was detectable (Fig. 3a and b). HPLC analyses demonstrated serum IgA to be mainly monomeric (< 5% dimeric IgA, no polymeric IgA),

whereas both SIgA preparations consisted of dimeric IgA (no detectable monomeric or polymeric IgA). Incubation of polymorphonuclear cells (PMN), from either Tg mice or humans with serum IgA-opsonized bacteria efficiently initiated phagocytosis, which was blocked by preincubation with mAb, a mAb recognizing the FcαRI IgA binding site (Shen L., *et al. J. Immunol. 143*, 4117-~~4112~~ 4122 (1989)). SIgA was unable to initiate phagocytosis (Fig. 3c-f), and PMN of NTg mice did not exhibit phagocytosis of either serum- or SIgA-coated bacteria. The observation that PMN were unable to phagocytose SIgA-coated bacteria was confirmed by experiments with V-gene matched chimeric serum- and SIgA antibodies directed against PorA of group B meningococci. Only serum IgA induced PMN-mediated phagocytosis of bacteria, whereas SIgA was inactive (Vidarsson et al., manuscript submitted).

Please replace the paragraph at page 19, line 20 through page 20, line 14, with the following amended paragraph:

Although it is well recognized from *in vitro* studies that ~~FcαRI~~ FcαRI represents a potent trigger molecule for phagocytosis, ADCC, and release of inflammatory mediators (Morton, H.C., *et al. Crit. Rev. Immunol. 16*, 423-440 (1996); Kerr. M.A. & Woof, J.M. Fcα receptors, in: *Mucosal Immunology,* eds. P.L. Ogra *et al.*, 213-224 (Academic Press, San Diego, CA, 1998)), its in *vivo* role is difficult to envisage, since the (secretory) IgA ligand is considered an anti-inflammatory antibody (Mestecky, J, *et al. Clin. Immunol. Immunopathol. 40, 105*-114 (1986); Mazanec, M.B., *et al. Immunol. Today 40,* 430-435 (1993); Lamm, M.E. *Annu. Rev Microbiol. 51,* 311-340 (1997); Brandtzaeg, P. *et al. Immunol. Today 20,* 141-145 (1999); Russell, M.W., *et al. Biochem. Soc. trans.* 25, 466-470 (1997)). To resolve this dilemma, we created an FcαRI Tg mouse model to study the role of human IgA and its receptor *in vivo*. Although FcαRI was not expressed in tissues from Tg mice, treatment with G-CSF induced FcαRI expression on liver Kupffer cells. Previous studies demonstrated FcαRI expression to be under strict regulation by cytokines, indeed. Granulocyte/macrophage colony stimulating factor (GM-CSF). interleukin (IL)-6, IL-1β, IL-8 and tumor necrosis factor (TNF)-α were reported to enhance PMN- or monocytes FcαRI levels (Morton, H.C., *et al. Crit. Rev. Immunol. 16*, 423-440 (1996); Weisbart, R.H, *et al. Nature 332,* 647-648 (1988); Nikolova, E.B. *et al. J. Leukoc. Biol.* 57, 875-882 (1995); Shen, L., Collins, *et al.* J *Immunol. 152*, 4080-4086 (1994)), whereas GM-CSF and TNF-α induced expression on Tg macrophages (Van Egmond, M., et al. *Immunol. Lett. 68, 83-87* (1999). Alternatively. injection of G-CSF might result in activation of Kupffer cells (Wisse, E. *et al. Toxicol. Pathol. 24,* 100-111(1996)). Substances like colony stimulating factor (CSF),

macrophage-colony stimulating factor (M-CSF), platelet-activating factor, Zymosan and endotoxin were shown to activate Kupffer cells24, with subsequent secretion of inflammatory mediators, including interleukins and TNF-α (Declcer, K. *Eur. J. Biochem. 192*, 245-261 (1990)). These latter cytokines might be responsible for the observed effect on FcαRI expression (Morton, H.C., *et al. Crit. Rev. Immunol. 16*, 423-440 (1996); Kerr. M.A. & Woof, J.M. Fcα receptors, in: *Mucosal Immunology,* eds. P.L. Ogra *et al.*, 213-224 (Academic Press, San Diego, CA, 1998); Hostoffer, R.W., *et al. J Infect. Dis. 170, 82-87* (1994)). Our observation that injection of TNF-α for two days triggers expression of FcαR1 on Kupffer cells supports an indirect effect of G-CSF (data not shown).